

Comment

capacity for emergency response among local health providers and populations.¹⁴ Finally, academics among the diaspora should work to quantify the important work that diaspora health workers are doing to gain further legitimacy as a force for good in global health. Whereas a plethora of scholarly work has focused on migration by health workers,¹⁻⁴ there is a dearth of high-quality research that investigates the contributions of diaspora health workers in health system strengthening in LMICs.

There is an urgent need for all stakeholders—governments in LMICs and high-income countries, non-profit organisations, academic institutions, and development agencies—to create a blueprint that lays down clear strategies for the organisation, preparation, and engagement of diaspora health workers in health system strengthening and emergency preparedness. Diaspora health workers deserve an integrated platform and organised opportunities to develop meaningful, long-term, and sustainable engagements that improve health in LMICs, during times of crisis and beyond.

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Oxygen saturation targets in infants with bronchiolitis

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Acute viral bronchiolitis is associated with lower respiratory tract infections in infants. Although generally self-limiting and managed in the community, acute viral bronchiolitis is the most common cause of hospital admission in infants younger than 12 months of age, and is associated with substantial morbidity and health-care costs. Admissions of infants to hospital for bronchiolitis have increased in the past 20 years for reasons that might be multifactorial, although the use of pulse oximeters and insufficient evidence and clarity about levels of tolerable hypoxaemia are thought to be associated with increased admission rates.¹ Additionally, duration of hospital stay seems to be determined by the

requirement for oxygen supplementation, even when feeding problems have resolved.² National guidelines in the USA³ and UK⁴ differ in their recommendations for supplemental oxygen to target acceptable saturations (SpO₂) of 90% or higher, or 94% or higher, respectively. An observational study in bronchiolitis⁵ previously suggested that length of stay could be reduced when lower oxygen cutoffs were chosen, setting the stage for the randomised BIDS trial now reported by Steve Cunningham and colleagues in *The Lancet*,⁶ which provides welcome evidence about the use of supplemental oxygen and oxygen saturation targets in bronchiolitis.

BIDS reports findings from a multicentre randomised equivalence trial of 615 infants aged between 6 weeks and 12 months, who presented to eight paediatric hospitals in the UK with bronchiolitis. These infants were randomly assigned to be monitored either by standard oximeters (n=308), or by modified oximeters (n=307) which had a skewed algorithm that displayed an SpO₂ reading of 94% when the measured value was 90% (with adjusted values for SpO₂ 85–100%). Supplemental oxygen was given to all infants with an SpO₂ reading lower than 94% on their assigned oximeter.

The median time of resolution of cough (the primary outcome) was 15 days for both groups (95% CI for difference –1 to 2), which was within the limits of equivalence. As expected, compared with the standard group, fewer infants in the modified oximeter group needed supplemental oxygen (169 [56%] vs 223 [73%]), and, when required, supplementation was for a significantly shorter duration (5.7 h vs 27.6 h) and the infants were fit for discharge significantly earlier (30.2 h vs 44.2 h). More unexpectedly, infants in the modified group returned to adequate feeding a median of 2.7 h sooner, were perceived to return to normal by their parents 1 day earlier, and had fewer readmissions to hospital within 28 days compared with those in the standard group. Adverse events did not differ between groups. The authors conclude that children with bronchiolitis could be managed with an oxygen saturation target of 90% or higher, instead of 94% or higher, with no short-term safety implications. This would result in earlier discharge home from hospital with the potential for health-care-cost reduction and improved quality of life for parents.

The primary outcome chosen by Cunningham and colleagues⁶ (resolution of cough) was unusual for clinical trials of bronchiolitis, although duration of cough is perceived to be important by families.⁷ The association between duration of cough and degree of hypoxaemia is not established, and it is interesting to speculate whether the results of cough duration would have been any different if an even lower saturation cutoff was chosen. Cunningham and colleagues suggest a potential interaction with airway inflammation, and it is also possible that cough might become more frequent with worsening hypoxia given the association between cough frequency and altitude⁸ and the as yet unexplained association between nocturnal cough and obstructive sleep apnoea reported in adults.⁹ Of the other outcomes

measured, the time to sufficient feeding and frequency of apnoea were possibly more discerning outcomes that could have been affected by hypoxia. The parental perception of return to normalcy might be biased by early discharge home, but, like readmission to hospital, would also reflect the parental level of concern about the infant.

Although Cunningham and colleagues' study⁶ provides convincing evidence that reduced oxygen saturation targets in bronchiolitis are safe in the short term, unfortunately the longer-term neurocognitive and behavioural outcomes are unknown. On one hand, the likely safety of the lower oxygen saturation target is supported from a physiological perspective because the oxygen–haemoglobin dissociation curve predicts that the actual oxygen delivered to tissues is unlikely to be very different with an oxygen saturation target of 90% instead of 94%, although risk factors such as fever and acidosis need to be taken into account. In addition, intermittent desaturation episodes of short duration (up to 6 s) have no adverse consequences in infancy.¹⁰

On the other hand, intermittent hypoxia over a prolonged period of months to years, as in sleep disordered breathing and long-term hypoxaemia due to altitude or congenital heart disease, has been associated with detrimental effects on long-term neurocognitive outcomes in children.¹¹ The resulting quandary is in clinical situations such as bronchiolitis or asthma, which lie somewhere between these two ends of the spectrum in terms of duration of lower saturations, when the longer-term safety of lower saturation targets falls into an evidence-free zone. When the American Academy of Pediatrics bronchiolitis guidelines³ were published in 2007 suggesting 90% as the acceptable saturation cutoff, Bass and Gozal¹² raised concerns about the potential detrimental effects on cognitive and behavioural outcomes, and concerns among paediatricians continue to be raised.¹³

Findings from BIDS⁶ also raise questions about the use of supplemental oxygen in other acute hypoxic states, such as exacerbations of asthma and community-acquired pneumonia. The decision about acceptable oxygen saturations for these disorders is also based on expert opinion and becomes a matter of clinical judgment, availability of health-care resources, and cost implications. Cunningham and colleagues have done a commendable job in bringing robust evidence with far-reaching implications to an area previously governed



by expert opinion; however, we urge consideration of long-term neurobehavioural follow-up of randomised trials such as BIDS, to shed light on the nagging question that remains.

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Multimodal treatment of non-small-cell lung cancer

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In *The Lancet*, Miklos Pless and colleagues¹ report a prospective randomised trial of induction chemotherapy followed by accelerated radiotherapy and surgery, compared with induction chemotherapy followed by surgery, to treat patients with stage IIIA/N2 non-small-cell lung cancer. 232 patients were enrolled in 23 study centres and were randomly assigned to the study groups in a 1:1 ratio. Median event-free survival, the trial's primary endpoint, was similar in the two groups (12·8 months, 95% CI 9·7–22·9 in the chemoradiotherapy group and 11·6 months, 8·4–15·2 in the chemotherapy group), as was overall survival (37·1 months [22·6–50·0] and 26·2 months, 19·9–52·1, respectively). In the chemoradiotherapy group around 10% more patients had complete R0 resections (90 [91%] vs 76 [81%]). The investigators conclude that trimodal therapy might not be needed in this subgroup of patients, and that a combination of induction chemotherapy and definitive surgery would be sufficient. Is this conclusion correct?

The number of patients in Pless and colleagues' trial¹ was insufficient to show non-inferiority between the two strategies and potentially to rule out a 5% difference in 5-year survival, which is generally induced

by differences in clinical response, pathological complete response, and R0 resection rates in larger populations. The trial was powered to detect a median increase in event-free survival by 6 months with radiotherapy, corresponding to a hazard ratio of 0·67. The likelihood of stopping a trial for futility falls tremendously with a decrease in the assumed treatment effect as the alternative hypothesis. The assumption of a hazard ratio of 0·8, therefore, would have been more realistic. Unfortunately, the number of patients with stage III non-small-cell lung cancer who are treated in prospective randomised trials is currently much too small to give clearer recommendations and to define the optimum treatment approach with much more precision.^{2–5}

The authors used sequential chemotherapy followed by accelerated radiotherapy instead of concurrent chemoradiotherapy, and noted a rather small difference in the pathological complete response, from 12% in the chemotherapy group to 16% in the chemoradiotherapy group. Trials on intensive neoadjuvant concurrent chemoradiotherapy have found rates of about 30%.^{6–8} In view of the favourable overall survival of patients